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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,779	04/20/2001	Amin I. Kassis	U0381-00001	2010

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DUANE MORRIS, LLP
IP DEPARTMENT
30 SOUTH 17TH STREET
PHILADELPHIA, PA 19103-4196

EXAMINER	
HANLEY, SUSAN MARIE	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/839,779	KASSIS ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-92* is/are pending in the application.

4a) Of the above claim(s) *55-58,64-67,69-75,81-84 and 86-92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-54, 59-63, 68, 76-80 and 85-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 23-41, 43-45 and 47-49 have been cancelled by the amendment filed 4/25/05. New claims 59-92 have been added. In view of the previously required election, claims 55-58, 64-67, 69-75, 81-84 and 86-93 are withdrawn from further examination. Applicant is directed to the Response filed July 16, 2002 wherein the R1 specie "gamma emitter" was elected. "Boron cage," as in instant claims 67 and 84, was not elected and therefore stands withdrawn.

Response to Arguments

Applicant's arguments filed 4/25/05 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 50-53, 59-63 and 68 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Pastan (US 5,489,525) in view of Haugland (US 5,316,906) and Hansen (US 5,851,527), Lebioda et al. (US 5,763,490), Mertens (US 5,021,220) and Christenson (US 4,107,285).

Applicant argues that claim 50 does not encompass an enzyme-conjugated antibody-based method but is now drawn to a method wherein an endogenous enzyme cleaves the prosthetic group from the prodrug in the extracellular space of the tumor. Applicant asserts that said enzyme is produced naturally by said tumor. Applicant further argues that the prior art does not teaching or suggest that compounds recited in claim 50 could be administered to a patient bearing a tumor or that such compounds would be localized within the tumor. Applicant argues that Haughland teaches the use of said compounds *in vitro* and that Pastan and Hansen rely on the use of an antibody-linked enzyme for the localization of the anti-tumor agent at the tumor site. Applicant asserts that Lebioda discloses that PAP is

secreted by the prostate throughout the body of the patient and this disclosure does not provide the skilled artisan with motivation to believe that the compounds of claim 50 would be selectively localized within a solid prostate tumor.

Responding to Applicant's argument that the claimed method does not encompass an enzyme-conjugated antibody-based method, the claim language is "open" due to the employment of the word "comprising." Therefore, the method steps of the claimed invention are not limited to those that are expressly put forth in the instant claims. Therefore, prior art that meets the express claim limitations and further discloses additional steps that do not teach away from the claimed method. In the instant case, the combined references teach the localization of radiolabled compounds of claim 50 at tumor sites. It is also known from Lebioda that prostate tumors secrete PAP which also cleaves the prostatic group of the claimed compounds. The addition of the antibody-linked enzyme is allowed to the open claim language of the instant application. The result of the addition of the antibody-linked phosphatase means that two sources of phosphatase, one endogenous and the other exogenous, would be available to cleave the prosthetic bonds of the claimed compounds.

Responding to Applicant's argument that an enzyme that cleaves the prosthetic groups is produced naturally by said tumor and that that Lebioda discloses that PAP is secreted by the prostate throughout the body of the patient and this disclosure does not provide the skilled artisan with motivation to believe that the compounds of claim 50 would be selectively localized within a solid prostate tumor, Applicant is directed to the full disclosure by Lebioda, wherein he states that the concentration of hPAP in a healthy body, the vast majority of hPAP is contained in the reproductive system "However, as prostate cancer develops, the cancer cells spread throughout the body secreting large quantities of hPAP enzyme. Level of the hPAP enzyme in blood serum have been used for monitoring the stage of prostate cancer for many hears, thus the well known PAP test for prostate cancer" (bridging paragraph between columns 1 and 2). Thus, Lebioda acknowledges that endogenous PAP spreads throughout the body *as the cancer cells spread* and that this is a known measure for prostate cancer.

Thus, the ordinary artisan would have realized that the pathology of the disease governs the concentration of PAP during the progression of the cancer. However, the ordinary artisan would have known that as the PAP spreads, its concentration would diminish compared to the PAP at the site of the tumor. Therefore, the ordinary artisan would have had a reasonable expectation that the compounds of claim 54 would undergo cleavage of the prosthetic group and localize the product at the site of the production of PAP, the tumor, since it is highest in concentration at the tumor site. Furthermore, the instant claims do not specify at what point during tumor progression that the claimed method should take place. Nor do the instant claims specify a particular level of radioactivity deposited at a given tumor site at any given time of the development of the cancer. According to the instant disclosure, the claimed invention would be subject to the same effect since the instant invention depends on the cleaving ability of endogenous PAP.

Responding to Applicant's argument that Haughland teaches the use of said compounds *in vitro*, Applicant is directed to col. 4, lines 48-55, wherein Haughland teaches that the disclosed substrate are suitable to detect the activity of a wide variety of enzymes and enzyme-related analytes . . *in vivo*.

Claims 54, 76-80 and 85 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Pastan (US 5,489,525) in view of Haugland (1995), Haugland (US 5,316,906) and Hansen (US 5,851,527), Lebioda et al. (US 5,763,490), Mertens (US 5,021,220) and Rose (US 5,816,259).

Applicant argues that claim 54 does not encompass an enzyme-conjugated antibody-based method but is now drawn to a method wherein an endogenous enzyme cleaves the prosthetic group from the prodrug in the extracellular space of the tumor. Applicant asserts that said enzyme is produced naturally by said tumor. Applicant further argues that the prior art does not teaching or suggest that compounds recited in claim 54 could be administered to a patient bearing a tumor or that such compounds would be localized within the tumor. Applicant argues that Haughland (catalog) teaches the use of said compounds *in vitro* and that Pastan and Hansen rely on the use of an antibody-linked enzyme

for the localization of the anti-tumor agent at the tumor site. Applicant asserts that Lebioda discloses that PAP is secreted by the prostate throughout the body of the patient and this disclosure does not provide the skilled artisan with motivation to believe that the compounds of claim 54 would be selectively localized within a solid prostate tumor.

Responding to Applicant's argument that an enzyme that cleaves the prosthetic groups is produced naturally by said tumor and that that Lebioda discloses that PAP is secreted by the prostate throughout the body of the patient and this disclosure does not provide the skilled artisan with motivation to believe that the compounds of claim 54 would be selectively localized within a solid prostate tumor, Applicant is directed to the full disclosure by Lebioda, wherein he states that the concentration of hPAP in a healthy body, the vast majority of hPAP is contained in the reproductive system "However, as prostate cancer develops, the cancer cells spread throughout the body secreting large quantities of hPAP enzyme. Level of the hPAP enzyme in blood serum have been used for monitoring the stage of prostate cancer for many hears, thus the well known PAP test for prostate cancer" (bridging paragraph between columns 1 and 2). Thus, Lebioda acknowledges that endogenous PAP spreads throughout the body *as the cancer cells spread* and that this is a known measure for prostate cancer. Thus, the ordinary artisan would have realized that the pathology of the disease governs the concentration of PAP during the progression of the cancer. However, the ordinary artisan would have known that as the PAP spreads, its concentration would diminish compared to the PAP at the site of the tumor. Therefore, the ordinary artisan would have had a reasonable expectation that the compounds of claim 54 would undergo cleavage of the prosthetic group and localize the product at the site of the production of PAP, the tumor, since it is highest in concentration at the tumor site. Furthermore, the instant claims do not specify at what point during tumor progression that the claimed method should take place. Nor do the instant claims specify a particular level of radioactivity deposited at a given tumor site at any given time of the development of the cancer. According to the instant disclosure, the claimed

invention would be subject to the same effect since the instant invention depends on the cleaving ability of endogenous PAP.

Responding to Applicant's argument that Haughland teaches the use of said compounds *in vitro*, Applicant is directed to Haugland (US 5,316,906) at col. 18, lines 48-52, wherein Haughland teaches that the disclosed substrate are used in a human patient to detect a small-cell carcinoma.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

JEAN C. WITZ
PRIMARY EXAMINER

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Hanley
Patent Examiner
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